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Lyme disease presenting as prolonged pyrexia of unknown origin

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Borreliosis includes within its definition both relapsing fever and Lyme disease. Relapsing fever has been recognized in our province since at least the 1930s [1] and is thought to be caused by *Borrelia hermsii*, which is transmitted by the soft tick *Ornithodoros hermsii*. Anecdotes of relapsing fever are reported on an almost yearly basis in British Columbia and Alberta, although few of these cases are published [2], and one of the largest recognized outbreaks of tick-borne relapsing fever in North America was recognized in the Browne Mountain area of Washington state, in close proximity to the British Columbia–Washington border [3]. In addition, Lyme disease has been recognized among British Columbians, although travel to other endemic areas is a feature in the history of most patients. Whereas the clinical manifestations of Lyme disease are now well detailed for both children and adults [4,5], a relapsing fever pattern or prolonged fever of unknown origin have not been published in the pediatric medical literature. We here describe an illness consisting of prolonged fever of unknown origin which developed in a child who acquired an endemic *Borrelia burgdorferi* infection in British Columbia.

A 13-month-old-female from central British Columbia developed a right forearm rash 2 weeks after an expedition to a lake in central British Columbia in late June. The parents recalled an 'insect bite' at the site of the dermatopathy, although a specific insect could not be defined. The rash was described as having a pale center and a red expanding circular edge. Coincident with the disappearance of the rash after 3–4 weeks, a fever developed and was measured maximally at approximately 40°C orally. The child received oral amoxycillin during the time when the fever persisted but appeared to have a moderate anaphylactoid reaction consisting of rash and listlessness. Although an antibiotic allergy was considered, the child had received oral amoxycillin on one occasion previously without side effects. The patient subsequently received oral cotrimoxazole and the febrile illness resolved over 2 weeks. On a weekly basis thereafter, however, and for the 6 subsequent months, the fever recurred,

lasting for 1–3 days and reaching 38–39°C orally. The febrile episodes were commonly accompanied by nausea and transient diarrhea. During this interval, the patient received several antibiotic courses, including cotrimoxazole and cefaclor for presumed urinary tract and middle ear infections. Antibiotic use, however, did not seem to affect the subsequent reappearance of the febrile illness. Although the forearm rash had completely disappeared without local residua, both legs and arms developed areas of eczematoid rash.

Laboratory data during the weekly illnesses were generally not helpful in providing a diagnosis, although two immunofluorescence antibody (IFA) titers to *B. burgdorferi* were both recorded as 1/256, at 2 and 3 months after the onset of illness. The family history was considerably complicated by the diagnosis of an inherited mitochondrial disorder in the father (including cardiomyopathy) and two siblings. Furthermore, the mother had recurrent urinary tract infection and the father required a right nephrectomy because of a complicated ureteral obstruction. There was no history of travel outside British Columbia.

The child was admitted to our children's hospital 6 months after the onset for investigation of the fever recurrences and an apparent failure to thrive in the context of the familial history of metabolic disease. A change in weight from 50th percentile (birth) to 5th percentile was observed. The child was afebrile at the time of admission and the last febrile episode had ceased 2 days before. Physical examination could not determine a focus for infection. There was no evidence of joint, central nervous system or cardiac disease. Laboratory investigations revealed: white blood cell (WBC) $10.0 \times 10^9/L$ (60% lymphocytes), hemoglobin 112 g/L, and platelets $300 \times 10^9/L$. Serum electrolytes, creatinine, lactate, liver and muscle enzyme profiles and amino acids were within the normal range. Both electrocardiogram and echocardiogram were normal. A repeat of the *B. burgdorferi* serology once again revealed an IFA titer of 1/256. An IFA titer to *B. hermsii* was less than 1/128. Western blot serology using *B. burgdorferi* antigen demonstrated immune recognition of seven polypeptides in addition to the flagellar (41 kDa), OspA and OspB antigens.

Fever was not recorded during 5 days in hospital but returned 7 days later and again recurred on a weekly basis. Oral erythromycin was administered by the seventh month and continued for 10 days. The child was afebrile during the antibiotic course and has remained so after cessation of the same, apart from a single episode of fever associated with a urinary tract infection. The eczematoid rash disappeared after the erythromycin treatment and has not recurred.

We believe that this child's illness was caused by infection with *B. burgdorferi*, or a very similar bacterium, on the basis of the history of the erythema chronicum migrans-like lesion following an insect bite which preceded the recurrent febrile illness and the serologic profile [6]. The pattern of fever, although recurrent, did not typify the usual descriptions of relapsing fever [7]. Rather, this illness would have been more accurately classified as a 'fever of unknown origin'. The response to erythromycin is also consistent with borreliosis. Furthermore, we postulate that the amoxicillin-associated anaphylaxis and the eczematoid rash were probably a Jarisch-Herxheimer reaction and a chronic *Borrelia* dermatopathy respectively.

Fever is a relatively common symptom in pediatric Lyme disease. Williams et al. [5] found fever (>101°F) to be present in approximately one-half of all patients. In addition, the latter investigators found that the common clinical characteristics included erythema chronicum migrans-like rash, 'flu-like' symptoms, arthritis/arthralgia, and a history of tick bite. A prolonged and recurrent febrile illness, as witnessed for our patient, has not been described among children. Intermittent and recurrent fever is, however, a hallmark of the relapsing fever illnesses that are caused by non-*B. burgdorferi* borreliae, but the frequency of such recurrences is generally 1–5; again very unlike our patient [7]. The *Borrelia* serology for our patient was not supportive of *B. hermsii* infection.

Fever of unknown origin has long been studied, especially in adults, and the need for a definition which is based on length of undiagnosed illness has been proposed. The addition of Lyme disease to the list of etiologic agents possibly associated with fever of unknown origin would only have been possible over the last decade, when the causative bacterium was discovered and when the laboratory diagnosis could be more certain. Indeed, Kazanjian [8] attributed fever of unknown origin to Lyme disease in 1 of 86 patients in a contemporary series. Nevertheless, the clinical course of our patient was unusual, given the especially prolonged course of the febrile illness. It is conceivable that similar presentations may become more numerous as experience with pediatric Lyme disease increases.

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Disseminated mucormycosis due to *Absidia corymbifera* in a patient with inflammatory bowel disease

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Mucormycosis is a rare fungal disease principally caused by species of the order Mucorales, family Mucoraceae (*Rhizopus*, *Rhizomucor*, *Absidia* and *Mucor*) [1]. This infection is usually seen in patients with certain underlying diseases and predisposing conditions. One of the most important features of the disease is that diagnosis is rare ante mortem, since signs and symptoms are non-specific, and the clinical course is often fatal, especially in disseminated forms. However, the infection is potentially curable with systemic administration of amphotericin B, aggressive surgical debridement, and control of the underlying disease. We report a disseminated form of mucormycosis caused by *Absidia corymbifera*, in a patient under treatment with steroids and cytostatic agents because of inflammatory bowel disease.

A 60-year-old man was admitted to the hospital on 12 January 1995, following a 14-day history of